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A CLINICAL CLASSIFICATION ON ASTHMA BASED UPON A REVIEW OF SIX HUNDRED AND FORTY-EIGHT CASES.¹

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It is clearly recognized today that asthma is always a symptom and never a disease as such. The diagnosis is usually made by the patient. The term "asthma" is here used to include all those cases in which a type of dyspnea characterized by difficult inspiration or expiration, or both; "wheezy" breathing is the predominant symptom. Such breathing occurs in a variety of conditions. The patient with a typical barrel chest full of squeaks and musical rales over which the breath sounds are prolonged usually has asthma, but his diagnosis should be pulmonary emphysema. Bronchial asthma is a loose term which is ordinarily applied to those patients with asthma in whom the physical examination between the attacks is essentially normal. As to the mechanism by which this peculiar type of dyspnea is produced we know little, although the theory of bronchial spasm with edema of the mucous membrane seems adequate.

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In the study of each case of asthma at least two factors in its cause are important. There is for each case of asthma an underlying basis the nature of which is quite unknown, except that it tends to be inherited, especially in those cases in which the asthma is due to foreign proteins. This basis may be referred to as the "asthmatic state" which underlies not only the various forms of asthma but such other conditions as hay fever, food and drug idiosyncrasies and certain cases of urticaria, angioneurotic edema, eczema, etc. On top of this basis recent investigation has identified a variety of types of asthma which it is the purpose of the present paper to review, with particular reference to their relations one with another.

The simplest and most obvious classification already discussed, especially by Walker and by myself, divides asthmatics into two main groups: First, those sensitive to foreign proteins in which the cause is outside of the body (extrinsic), and second those not sensitive where the cause is inside of the body (intrinsic).

During the past three years patients with asthma have been studied in the clinic for anaphylaxis at the Massachusetts General Hospital and in private practice. The accompanying chart shows an arrangement of these cases and is an attempt to demonstrate the clinical relation in the various groups. In the management and treatment of cases this chart has been found to be of great practical value.

Foreign proteins may enter and act upon the body in several ways, particularly through the respiratory tract, as in Groups A and B of the chart and through the gastro-intestinal tract, as in Group C.

Group A. POLLEN HAY FEVER AND ASTHMA. Group A represents cases which were sensitive to the plant pollens. There were 71 cases of early hay fever (sensitive to the graminaceæ, timothy, red top and June grass), 227 cases of late hay fever (sensitive to the compositæ ragweed) and 49 cases of double hay fever—a total of 347 cases of hay fever. (These cases of simple hay fever are not included among the 648 cases of asthma.) Pollen asthma describes the asthma which occurs as an aggravation of hay fever. Pollen asthma must, in its pure form, be limited in its dates of onset and subsidence to the true hay fever season. Pollen asthma occurred in only 9 cases of early hay fever (12.6 per cent), in 81 cases of late hay fever (35.7 per cent) and in 9 cases of double hay fever (18.3 per cent), "and in a total of 99 cases (28.5 per cent) of all types of hay fever." This is the most typical form of asthma known: the easiest to diagnose and the simplest to treat. Desensitization with pollen extract relieves this asthma even better than it relieves hay fever.

Some cases which give a history compatible in the early stages with a pollen asthma—and later with a complicated pollen asthma—will say that still later, after the apparent end of their usual fall attack, they will have other attacks during the winter and spring. It is obvious that these other attacks of asthma can have no relation to any pollens and must therefore be due to bacterial action or in certain cases to some reflex action. It might be presumed that other foreign proteins in dust or food might perhaps be responsible for the later attacks in such patients, and, indeed, 7 patients reacted positively to one or other cereal proteins and 1 of them to eggs as well. However, in the 7 cases the removal of the corresponding food had no effect on the asthma.

The diagnosis of pollen asthma can be made in most cases by a careful history and without skin tests. Occasionally a case of supposed pollen asthma was found that failed to react to pollens. Study, however, revealed the fact that such patients had no eye or nose symptoms preceding their asthma, which of course emphasizes the importance of care in history-taking.

Up to this point the physical examination of these patients between their attacks of asthma is always normal. As the asthma progresses, as the attacks become longer and the intervals shorter, evidence of a secondary pulmonary emphysema develops. This will be discussed at greater length later. Suffice it to say that of the 99 cases of pure pollen asthma, 23 cases went on to develop perennial asthma, and 13 of these had emphysema. Two cases which had late hay fever and also had a perennial asthma had never been worse during the fall, so that in them a diagnosis of pollen asthma was not made.

Group B. DUST ASTHMA. Group B is a group closely related to Group A, and includes 76 cases of individuals sensitive to foreign proteins other than the pollens, but is confined to those cases in which the contact is by way of the respiratory tract, and in which the exposure is to proteins in dust. Here are 45 cases of horse asthma, 9 of which were sensitive to the pollens as well and one of which reacted to egg-white. In addition there are 8 cases of asthma due to feathers, 8 cases of asthma in bakers and housewives due to wheat flour dust, 1 case due to cats and 1 to dogs, 1 to coffee, and 11 cases of asthma due to some unknown dust, only 6 of which had positive tests, and these tests were incompatible with the history. In this last group of 11 cases this diagnosis was made because of the peculiar circumstances: a theater, a musty house or a farm which invariably precipitated the attack. It is felt that more comprehensive tests might have revealed the offending protein, for as long as the patient avoided the particular circumstances there was no asthma. Walker, quoting Goodale, has lately defined such cases as reflex in nature (through the olfactory nerves).

The 8 cases of asthma from wheat flour dust are of great interest. They were all in bakers. In spite of the fact that they gave satisfactory tests to the wheat proteins they had no symptoms at all referable to eating white bread. Symptoms developed only during or shortly after exposure to wheat flour in the form of dust. In other words, symptoms were caused only by contact through the respiratory tract. Treatment, however, included the withdrawal of cereals in the diet, as a cumulative action is a distinct possibility. Cases of susceptibility to other dusts, such as orris-root powder, rice powder, rabbit, guinea-pig and miscellaneous hair, perhaps leather dust and a variety of others, should be mentioned for the sake of completeness, although in the present study no such case was identified. In an analysis of 198 cases of vasomotor rhinitis susceptibility to orris-root powder was found in 13 (6 per cent), but none of the patients had asthma.

As in the case of pollen asthma, so horse or dust asthma may readily be complicated by bacterial infections to a greater or less extent, and these complications may ultimately produce emphysema. In this Group B, 16 cases in the total of 76 were so complicated and 10 went on to develop perennial asthma, and 8 of them emphysema as well.

Group C. FOOD IDIOSYNCRASY. Group C represents those individuals who are obviously poisoned by certain definite foods or food combinations. This poisoning manifests itself by asthma, by urticaria, by angioneurotic edema or occasionally by violent gastro-intestinal upsets or by eczema.

In 19 cases, or only 3 per cent of the 648 cases of asthma, proteins in food were considered to be the cause, not only because each patient gave a well-marked test to the protein in question, but also because the patient's symptoms were definitely relieved when the particular food was eliminated.

These 19 cases were sensitive in 10 cases to egg, in 4 to wheat, in 2 to meat and in 1 each to nuts, fish and milk; 4 cases were sensitive each to a number of different foods, the most frequent combination being to eggs and wheat. Eleven of these 19 cases were in children. It so happened that no case of food asthma in this series was found which had a complicating bacterial asthma.

Thirty-five cases of urticaria and 6 cases of angioneurotic edema have been tested² but no case of either urticaria or angioneurotic edema was found to have asthma.

Twenty-nine cases of eczema were tested and 5 of these also had asthma which seemed to come and go with the eczema. Four of these 5 cases had positive tests each to one or more food proteins.

Group D. BACTERIAL ASTHMA. Group D represents perhaps the most common group, which can be subdivided as follows:

² For results see paper on Skin Tests with Foreign Proteins, which will appear in an early issue of this Journal.

1. Where asthma dates from a definite acute respiratory infection, 17 cases (13 adults and 4 children).

2. Eighteen cases in which there is each year a rather sharp and severe but relatively short attack of asthma occurring with the first cold spell of autumn and often recurring with the violent changes in temperature in March. Seven of these 18 cases were in male adults over thirty-five years old.

3. Thirty-five cases of "winter" asthma where the symptoms are closely associated with the cold weather of New England; are persistent and present practically constantly until the spring. Any fresh cold makes them markedly worse. All of these cases were in adults. Their separate classification is perhaps artificial, since many cases closely resemble the cases of perennial asthma to be discussed later. The group should be recognized, however, because a change to a warmer climate is an efficient and valuable treatment.

4. Bacterial asthmas in children, 38 cases, which come on most often after a cold and last for variable periods—the important point being that between the attacks these children are quite well. In case they are not quite normal between the attacks and still retain a certain amount of wheezing and dyspnea on exertion, it is usually found that they have mild emphysema, large peribronchial lymph nodes or some other organic cause for the symptoms. In each of these subgroups the tests are ordinarily negative, but 7 children have been added in spite of a positive test, since nothing in their story seemed to agree with the test.

Group E. REFLEX ASTHMA. While it is usually accepted that in many cases asthma depends upon the action of foreign proteins, yet in other cases the relation of proteins to the etiology is much less clear. In many of these latter some organic condition outside of the respiratory tract can be discovered and can be assumed to be indirectly responsible for the asthma, although the precise mechanism of its effect is usually unknown.

In the present study 78 cases are placed under the heading of reflex asthma. In 16 of these cases, mostly in children, bad nutrition was considered to be the cause rather than the result of the asthma, largely because treatment directed toward the regulation and enlargement of the diet, but without attention to specific foods, caused a great relief of the asthma. In at least 4 cases the asthma was associated with and presumably due to a faulty posture with ptosis. In 4 cases with disturbances of the gastro-intestinal tract, asthma was associated with constipation, the relief of which relieved the asthma. In 9 cases with diseased tonsils, 1 with lung abscess, 4 with bad teeth, and 11 with chronic pulmonary tuberculosis the absorption of toxic material is easy to understand, as at least a contributory cause to poor general condition and asthma. In 8 cases various pelvic disturbances were associated with the asthma, including the menopause and pregnancy, and in 2 cases asthma was invariably associated with the catamenia.

Referring to the definition of the term asthma as given in the first paragraph of this paper, it is of interest to note that recently a patient was referred to the writer for asthma in whom a tumor, probably luetic in nature but of sufficient size to obstruct the breathing, was found in the bronchial mucous membrane.

In the group of reflex asthma also are placed 13 cases of nervous asthma in which excitement or association with some disagreeable undertaking (return to college, beginning summer work, preparations for a journey) was the exciting cause of asthma in these patients with a general nervous instability; and finally, in 5 cases asthma seemed to follow a long period of stress and strain. Several of these latter cases have been undoubted results of the war, and a prolonged period of rest and relaxation, without other treatment, has caused a great improvement.

One case of this type is that of a widow who, left entirely alone, broke down under the strain of settling her husband's estate, sending the children to school and trying to do all the housework when her servants abandoned her. With a complete rest and change of environment the asthma largely disappeared.

Perennial Asthma. It is obvious that as asthma progresses the attacks become more frequent and of greater duration, but as a diagnosis of emphysema cannot be made in these cases, this way-station in the chart is justified. It would only be confusing to attempt to trace here the origin of the many cases of perennial asthma: but for the treatment of each case, this origin must be traced, if good results are to be obtained.

In addition to 23 cases in Group A and 10 cases in Group B who have reached this stage of perennial asthma there is a group of 48 cases who state in their history that their asthma has from its start been chronic with comparatively short intervals between attacks. Most, if not all, of these cases are of bacterial origin—their skin tests are all negative. Their separate classification is artificial and perhaps unnecessary.

Emphysema. On the chart a horizontal line is drawn between perennial asthma and emphysema. This line represents the onset of a demonstrable organic change in the patient which will remain constantly present even though the patient is sure that he "is entirely well."

Such patients have dyspnea on exertion which is usually associated with wheezing. If they are examined at any time, even between their attacks of asthma, they will show a more or less barrel-shaped chest with rounded shoulders. The breath sounds are most often diminished in intensity and high pitched in quality. Musical, whistling or squeaky rales are almost always present or can be brought out if the patient coughs a few times. In well-marked cases the pulse is often of poor quality: there is usually some cyanosis depending on the amount of associated bronchitis; the pulmonic

second sound is accentuated, due to the increased intrapulmonary pressure, while the heart seems on percussion to be small, due to the overlying lung. Such patients suffer from a markedly increased dead space in their air passages and from a markedly diminished vital capacity due to the large amount of retained air which they cannot expel.

Such patients are prone to develop chronic infections of the bronchi which are very resistant to treatment, in that these infections aggravate the emphysema just as the emphysema aggravates them, so that a vicious cycle is promptly established.

Emphysema may be acute compensatory following a severe attack of asthma. It may be idiopathic—that is, may be itself the primary condition arising in an unknown manner and not following an attack of asthma, and finally it may obviously be a late secondary result of chronic asthma.

In this series a total of 136 cases are diagnosed emphysema. Thirteen have already been included under pollen asthma, 8 under dust asthma and 4 under reflex asthma. Of the other 111 cases 14 gave a positive skin test to one or more foreign proteins, ragweed pollen, horse-hair extract and the wheat proteins being the most common. These cases have not been included in other groups because there was no history of hay fever or horse asthma which might have justified the test-finding. Twenty-one of these 111 cases were acute and of less than two years' duration. Twenty-five cases followed a history of chronic asthma and were of over twenty years' duration.

That prolonged emphysema with its associated chronic bronchitis may lead to myocardial insufficiency and arteriosclerosis seems undoubted whether the cause depends upon the burden to the circulation added by the almost constant effort to breathe or whether the cause is referable to the absorption of toxic material from the bronchi. It is, however, difficult to tell in just how many cases the myocardium is damaged, so that no figures can be given here.

In the foregoing, 648 cases of asthma have been discussed and classified. In addition to the above, 47 cases, or nearly 7 per cent of the whole, remain to date unclassified, most of whom have not been seen since their first visit.

Treatment. Treatment depends, obviously, on the type of asthma from which the patient suffers. Treatment by removal of foreign proteins or by attempts to desensitize the patient to them is sufficient in certain cases. On the other hand the treatment of perennial asthma, for example, will never be satisfactory until the etiology of each case is worked out. In the cases classified below, the "line of organic change," no treatment will be entirely satisfactory, although much can be done for the patient's comfort. In the cases above the line everything possible should be done to prevent the progress of the disease downward, and the hope of success is not unreasonable.

The chief function of such a classification of asthmatics, as is described above is, of course, to aid in the treatment of these patients. As is seen, most of the cases of asthma have neither a basis of definite foreign proteid susceptibility nor have they any abnormality which might justify a diagnosis of "reflex asthma," so that most of the cases come under the heading of "bacterial asthma" or, at all events, are complicated by bacterial infection. The subdivisions of this great group of bacterial asthmatics as given here are made on an empirical basis, usually not founded on any definite scientific basis but simply depend upon clinical observations and characteristics. In practice, however, these subdivisions have been found to be of some importance in treatment.

Vaccines have come to play an even more important role in the treatment of asthma, although their value from the strictly scientific viewpoint is as yet unknown. If it is assumed that the attacks of asthma depend upon a low-grade focus of bacterial action, say in the bronchial tubes, and if the use of vaccines is found to relieve these symptoms, it may be assumed that this relief depends upon the irradiation, permanent or temporary, of this focus, and this irradiation in turn is probably caused by the production of an active immunity. The possibility that the patient may be sensitized to bacteria and that the results of vaccine treatment are good because of a production of desensitization is another theory. There is little or no scientific basis available to date to help us choose between these two theories. The second theory has been advanced largely because of the desire to correlate all these cases with the simpler and more obvious cases of pollen and other foreign proteid sensitiveness. At all events it should be borne in mind that vaccines produce their greatest effect, at least in other conditions than asthma, by producing an active immunity, and therefore it may be assumed that vaccines will work best in those cases of asthma whose attacks are isolated by fairly definite intervals of more or less complete freedom from symptoms.

Another point about vaccines: in a previous paper the writer attempted to show that vaccines do good in asthma only in case a local reaction is produced at the site of inoculation. This finding has been many times confirmed and in many cases has furnished a method by which the proper vaccine for treatment has been selected. This method consists roughly in making separate vaccines from each of the various organisms isolated from the patient's sputum and then giving small doses of each vaccine subcutaneously. In twenty-four hours the local reactions from one or two of these vaccines may be fairly definite (heat, redness and tenderness), while there will be no reaction from the other strains used. If this is found to be the case, treatment with the organisms producing the reaction will usually give satisfactory results, whereas if the other non-reacting organisms are used in vaccines the further doses can be tremen-

dously increased without producing either local reaction, aggravation or improvement of the symptoms.

The object of this paper will have been attained if it has emphasized that not only are there many forms of asthma, but also by proper classification and by proper selection of the form of treatment a great deal can be done for these unfortunate sufferers.

Conclusions. 1. A chart showing the interrelation of various groups of asthmatics is presented in the hope that it will prove of service in the classification of these patients.

2. The importance of a careful study of the patient, and especially of his history, is emphasized.

3. The importance of a proper classification and of a knowledge of the origin of asthma in any given case as a precursor to the successful treatment of that case is demonstrated.

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